

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

1-13. (Cancelled)

14. (Currently amended) A method for preparing a humanized antibody, wherein a framework region ("FR") in the humanized antibody is a FR naturally occurring in human antibodies, comprising the steps of:

- (1) obtaining a humanized antibody, wherein the humanized antibody has:
 - i) six ~~[[a]]~~ complementary determining regions ("CDRs") ~~region~~ ("CDR") of a first animal species; and
 - ii) eight FRs of a second animal species, wherein one or more amino acid residues in one or more of the FRs have been substituted to retain antigen binding ability, with corresponding amino acid residues in FRs of the first animal species, and wherein said second animal species is human;
- (2) conducting a homology search using a database of amino acid sequence of FRs naturally occurring in human antibodies ("natural FRs") in comparison with the amino acid sequence ~~of the FR in which amino acid residues have been substituted in step (1)~~, of the humanized antibody obtained in step (1), wherein the homology search is conducted over all 8FRs;
- (3) preparing a list of amino acid sequences of the natural FRs having the same as ~~or at least 80% homology~~ a high homology with the amino acid sequence of the FR, ~~in which amino acid residues have been substituted in step (1)~~, of the humanized antibody obtained in step (1),
- (4) selecting, from the list of step (3), a natural FR which has
 - i) at corresponding positions the same amino acid residues as the amino acid residues introduced by the substitution in step (1); and

ii) comprises an amino acid sequence that is the same as or has at least 80% homology ~~a high homology~~ with the FR sequence of the humanized antibody obtained in step (1);

(5) if the amino acid sequence of the FR, in which amino acid residues have been substituted in step (1), of the humanized antibody obtained in step (1) has one or more amino acid residues that are different from amino acid residues at corresponding positions of the natural FR selected in step (4), replace said different amino acid residues in the FR sequence of the humanized antibody obtained in step (1) with corresponding amino acid residues in the natural FR;

(6) constructing an expression vector expressing an amino acid sequence of the antibody obtained via steps (1) to (5);

(7) culturing cells comprising an expression vector constructed in step (6); and

(8) recovering from the culture the humanized antibody comprising the natural FR ~~from the culture~~ and 6 CDRs from the first animal species and wherein the recovered humanized antibody binds an antigen that is the same as the antibody from the first animal species.

15. (Previously presented) The method according to claim 14, wherein the first animal species is a non-human mammal.

16 - 17. (Canceled)

18. (Previously presented) The method according to claim 15, wherein the non-human mammal is selected from a mouse, rat, hamster, rabbit and monkey.

19. (Previously presented) The method according to claim 14, wherein all natural FRs belong to the same subgroup.

20. (Previously presented) The method according to claim 14, wherein the number of the substituted amino acid residues of the FR in step (1) is from one to ten.

21. (Previously presented) The method according to claim 14, wherein the number of the different amino acid residues in the FR in step (5) is from one to ten.

22. (Previously presented) The method according to claim 14, wherein the substituted amino acid residues in the FR in step (1) comprise an amino acid residue selected from amino acid residues responsible for canonical structure of the antibody, amino acid residues involved in the maintenance of the structure of CDRs, and the amino acid residues that directly interact with an antigen.

23. (Previously presented) The method according to claim 20, wherein the substituted amino acid residues in the FR in step (1) comprise an amino acid residue selected from an amino acid residue at position 71 of the heavy chain or at position 94 of the heavy chain.